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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/524,199

07/28/2005

Daniel Christopher Brookings

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07/16/2008

MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP

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EXAMINER

CHANDRAKUMAR, NIZAL S

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

07/16/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/524,199	Applicant(s) BROOKINGS ET AL.	
	Examiner NIZAL S. CHANDRAKUMAR	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 June 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 and 12-21 is/are pending in the application.
- 4a) Of the above claim(s) 12-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

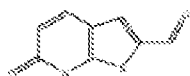
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|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>03/06/2008; 09/19/2005</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election of

Group 1, claim(s) 1-9, drawn to compounds of the core structure



in the reply filed on 05/08/2008 is acknowledged.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim 12-21 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 05/08/2008.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and dependent claims rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites a "linker atom or group", however the identity of a linker atom or group is not defined. Claim 1 also recites several moieties that are not clearly defined by the specification including Alk1, Cyl and "optional substituent". These groups are defined with exemplary language, as in Alk1: "when

Alkl is present in compounds of formula (1) as an optionally substituted aliphatic chain it may be an optionally substituted C 1-10 aliphatic chain. Particular examples include optionally substituted straight or branched chain C1-6alkylene, C2.6alkenylene, or C2.6alkynylene chains." The term "optionally substituted" is indefinite. Unless one knows what a substituent is, a determination of what these compounds are cannot be made. The specification does not fully elaborate the identity of these substituents. This rejection is not being made for breadth, which will be discussed (in *infra*). See MPEP 2173.05(d), for the use of exemplary language. The term "a linker atom or group" in all occurrences in the claims is interpreted to be a relative term which renders the claim indefinite. The term "a linker atom or group" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. What does Applicant intend by this term? Any atom or group has no limitations and is deemed vague and indefinite.

The claims are drawn to 'solvates, hydrates and N-oxides' without distinctly specifying the structure and composition of the compounds being claimed. Solvates, for example, are definite compounds with formula, such as C₉H₇N 0.25 HCl.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for some of the compounds of formula I, does not reasonably provide enablement for plethora of structures encompassed by the formula I. The specification does not enable any person

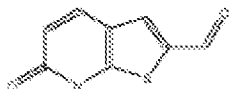
skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the relevant factual considerations.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). These include: (1) breadth of the claims; (2) nature of the invention; (3) state of the prior art; (4) amount of direction provided by the inventor; (5) the level of predictability in the art; (6) the existence of working examples; (7) quantity of experimentation needed to make or use the invention based on the content of the disclosure; and (8) relative skill in the art.

All of the factors have been considered with regard to the claims, with the most relevant factors discussed below:

The breadth of claims: The claims are drawn to compounds of the formula (*elected group, core structure shown below*)



The substituents on all the available 5-positions are layered with a variety of additional substituents encompassing millions of possible compounds. The substituents vary widely in size, molecular topology, properties such as acidity and basicity, rendering the breadth of the claims wide. The claims are also drawn to undefined solvates, hydrates rendering the number of conceivable structures large.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the art of organic and medicinal chemistry, it is noted that each embodiment of the invention is required to be individually assessed for viability.

The amount of direction provided by the inventor and the presence or absence of working examples: The direction and working example provided in the specification is limited. The specification has one scheme (page 30) relevant for making the core structure of the elected thienopyridine compounds. The guidance and direction present in the scheme is enabling for making compounds wherein Ra and Rb are hydrogens. Other substituents claimed for Ra and Rb, such as COOH group would be incompatible with chemistry necessary for introducing variables in other positions of the thienopyridine. The chemistry shown on page 36, (for 2-substituents (carboxylic acid derivatives)) would be incompatible in the presence of an Ra or Rb substituent such as COOH.

The specification does not provide citations (commercial or literature) for procuring the starting materials usable that could substitute for the lack of working examples with respect to non-enabled substitutions.

Though, there is enabling disclosure on page 30, for making L = N variables only, other possibilities for L are feasible without undue to experiment.

The claims are drawn to hydrates and solvates. But the numerous examples presented all failed to produce a hydrate or solvate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However... there is no evidence that such compounds exist..., the examples of the '881 patent do not produce the postulated compounds..., there is ... no evidence that such compounds even exist." The same circumstance appears to be true here: there is no evidence that solvates of these compounds actually exist; if they did, they would have formed.

With respect to potential use of the claimed invention, the disclosure in the specification is limited to generic statement that the compounds of the Examples have IC50 values (for p38 kinase) of around 1 micromolar.

The state and the predictability of the art: With regards to making of the compounds, in spite of major

advances in protecting group strategies and organic synthesis, the state of the art is unpredictable as to functional group compatibility during many chemical transformations. As discussed for one Ra or Rb possibility, one of ordinary skill in the art attempting to make applicant's compounds would be faced with trial and error experimentation to arrive at a viable chemistry sequence to introduce the many invariants present in the formula I. The existence of such unpredictabilities and uncertainties would prevent one of ordinary skill in the art from accepting the only process present in the specification on its face as universally applicable for all the substitutions claimed.

The quantity of experimentation: For the reasons presented above, there is a substantial gap between what is taught in the specification and what is being claimed. Given that the specification does not disclose any SAR with respect to biological activity or because there is no disclosure in the specification with regards to applicant's 'minimum pharmacophore' for inhibitory activity, it is not clear what specific embodiments would be required to inhibit kinases. As such, one of ordinary skill in the art would be faced with undue amount of experimentation to identify the compound(s) buried in the million possibilities encompassed by the formula.

The specification is enabling for compounds of the elected group wherein

Ra = Rb = H; and

in formula I Y is -CONH₂, -CONHet, -CON(R₂)Het, -CON(R₂)AlkHet or -COOAlk.

Deleting solvates, hydrates and N-oxide from the claim language would overcome 112-1 and 112-2 rejections corresponding to these terms.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

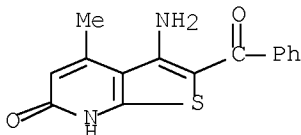
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and dependent claims rejected under 35 U.S.C. 102(b) as being anticipated by prior art.

Litvinov et al. Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya (1984), (8), 1869-70.

Litvinov et al. teach

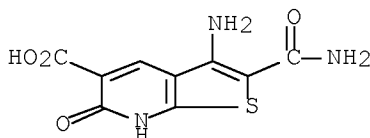


Corresponding to compound of the instant formula wherein

n is zero; L1 is covalent bond; Cy1 is H; L is an atom (N); Ra is alkyl; Rb is H; Y is substituted carbon (for the elected group this related to C=O connected to phenyl).

Likewise,

Dotsenko et al. Russian Chemical Bulletin (Translation of Izvestiya Akademii Nauk, Seriya Khimicheskaya) (2002), 51(8), 1556-1561, teaches



Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application

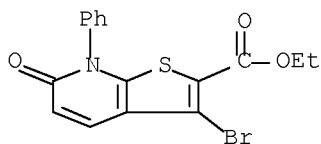
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filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 1 and dependent claims rejected under 35 U.S.C. 102(e) as being anticipated by Davis et al. (WO 2003033502, International filing date 10.16.2002).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

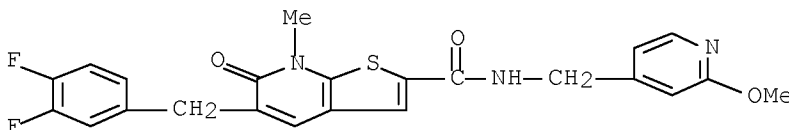
Davis et al. teach,



corresponding to compound of the instant claim wherein n is zero, L1 is a covalent bond, Cy1 is aromatic; Ra and Rb are Hydrogens; Y is C-COOEt in the elected group CO of the core structure is connected to alkoxy. The pictured formula I requires that L is at the minimum a divalent; though in the above structure Br corresponds to LAr of the pictured formula, one possible interpretation is that Ar is absent when L is a monovalent atom such as halogen or H.

Claims 1 and dependent claims rejected under 35 U.S.C. 102(e) as being anticipated by Wilson (US 6949651, provisional application date 08.13.2002).

Wilson et al teach



Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the

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conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-9 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of copending Application No. 10/518725, 10561052, 10561051, 10561050. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims of the cited applications and the instant claims are drawn to same or similar thieno[2,3-b]pyridine-6-one compounds and for the same alleged utility.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NIZAL S. CHANDRAKUMAR whose telephone number is (571)272-6202. The examiner can normally be reached on 8.30 AM - 4.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571 0272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nizal S. Chandrakumar

/D. Margaret Seaman/
Primary Examiner, Art Unit 1625